Ott. (J.)

PHYSIOLOGICAL ACTION OF GELSEMIA.

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GELSEMIA was first procured in a pure state by Prof. Wormley. Mr. Henry Kollock, C. L. Eberle, and Prof. Maisch also obtained it, but in an impure state. The alkaloid is always found combined with an acid called gelseminic. As an average of several experiments, Prof. Wormley states that there are about 3.20 grains of gelsemia in eight fluidounces of Tilden's fluid extract. Wormley said one-tenth of a grain of chloride of gelsemia given by the mouth in a cat caused frothing, in twenty minutes great weakness of extremities, walking with much uncertainty; in forty minutes extreme prostration, entire inability to walk, plaintive cries. Six hours after taking the poison the animal was comparatively well, although the gait was uncertain. Three days afterwards, in the same cat, one-eighth of a grain of gelsemia in shape of chloride caused in fifteen minutes great distress, moaning; in forty minutes great prostration, great difficulty in moving, the legs giving way; progression being as often backwards as forwards; pulse 230, very feeble; respiration gasping, greatly reduced; pupils dilated to fullest extent. Death in an hour and a half after taking the poison, without convulsions.

SURGEON GEN'L'S OFFICE
382
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Bartholow* experimented with an aqueous extract of gelseminum and a little gelsemia obtained from Wormley.

He concludes that in cold-blooded animals it acts on the nerve-centres, paralyzing the sensory ganglia, and afterwards the motor; that it does not affect muscular irritability of the peripheral nerve-fibres. In warm-blooded animals the same effects were observed, save only that the motor centres were the first attacked, instead of the sensory; that it kills through the respiratory apparatus; that in a pigeon it reduced the temperature from 107° F. to 104° F., and in a kitten from 102° F. to 98° F.; that there is no antagonism between it and strychnia; that it dilates the pupil. My gelsemia was made by Messrs. Hance Bros. & White, of Philadelphia. It was yellowish, odorless, with a bitter taste; concentrated sulphuric acid added to a small quantity of it produced a reddish solution, which when moderately heated passed into a fine purple, and nitric acid gave with it a greenish color. It undoubtedly contained some resin. The solution that I used was neutral, and each cubic centimetre contained one centigramme of gelsemia dissolved by acetic acid. On account of the small quantity of the alkaloid in my hands, I also made some experiments with Tilden's fluid extract, a concentrated tincture representing in each fluidounce four hundred and eighty grains of the root.

ACTION ON THE NERVOUS SYSTEM.

Exp. I.—Very large frog, received at 8.23 A.M. .02 gramme of gelsemia subcutaneously; remains quiet. 8.35 A.M., has a crouching attitude, sensibility much diminished. 8.50 A.M., .04 gramme subcutaneously. 9.35 A.M., .02 gramme subcutaneously. 9.50 A.M., the

* Practitioner, October, 1870.

lower jaw is commencing gradually to relax; moves about occasionally. 10 A.M., croaks and struggles some, suddenly turns himself on his back, in a state of convulsive movements; sensibility exaggerated; twitching of muscles of the extremities for a few minutes. 10.22 A.M., sensibility nearly lost, although movement retained. 10.35 A.M., animal dead. The peripheral end of sciatic irritable at forty-two centimetres Dubois coil; the gastrocnemius directly irritable at twenty-nine. Section of cord gives a slight twitch in extremities.

Exp. II.—Very large frog, received at 11.7 A.M. .06 gramme of gelsemia subcutaneously. 11.24 A.M., sensibility diminished. 12.20 P.M., sensibility very little; upon pinching makes vigorous movements; lies with extremities extended; muscles of lower jaw relaxing. 12.45 P.M., .02 gramme subcutaneously. 1.40 P.M., makes forcible movements of extension with posterior extremities; sensibility very small. 2.10 P.M., .02 gramme subcutaneously. 2.45 P.M., frog dead. Peripheral end of sciatic irritable at twenty-nine centimetres; muscles directly irritable at seventeen centimetres; spinal cord non-excitable; heart beating twenty times per minute.

The above experiments show that gelsemia produces loss of sensibility, want of co-ordination and paralysis of motor power, and finally death. The loss of sensation always precedes that of motion.

Exp. III.—Frog with right iliac artery and vein tied, received at 8.35 A.M. .04 gramme of gelsemia; hops away. 8.50 A.M., sensibility much diminished; 8.54 A.M., .02 gramme subcutaneously. 9.35 A.M., .02 gramme; sensibility greatly reduced; lower jaw hanging down; lies with extremities stretched out; loss of co-ordination. 10.5 A.M., suddenly struggles with posterior extremities. 10.22 A.M., sensibility nearly lost; can move when pinched. 10.23 A.M., dead. Peripheral end of sciatic on poisoned side is excitable at thirty-seven centimetres; on normal side at forty-three centimetres; no reflex action by irritating central end of sciatic; thrusting probe down the spine gives a few feeble twitches; the gastrocnemius on sound side by direct irritation responds at twenty-eight centimetres; the gas-

trocnemius of poisoned side is excitable at same distance of secondary coil from the primary.

This experiment shows that the poison attacks the sensory ganglia first, and then gradually paralyzes the motor ganglia; that it has no action on the muscular system.

Exp. IV.—Rabbit; at 4.25 P.M. received .01 gramme gelsemia per jugular. 4.27 P.M. to 4.31 P.M., .04 gramme gelsemia. After each injection there were convulsive movements. 4.33 P.M., the rabbit seems unable to move; feet slide from under him; muscles of neck seem especially weak, as head falls down on floor; rolls over on side occasionally. 4.40 P.M., convulsive movements of the fore extremities and muscles of lower jaw; the jaws snap together; violent expiratory movement, accompanied with a crying noise; pupil dilated. 4.41 P.M., animal dead; cord gives a few very feeble twitches on probe-thrust; motor nerves excitable; heart beating.

Exp. V.—Pigeon; at 12.35 P.M., received subcutaneously 2.5 cubic centimetres of Tilden's fluid extract of gelsemium. At first he walks off with a slight limp in the leg which received the poison; closes his eyelids frequently; remains stationary, with commencing ruffling of feathers. 12.40 P.M., sits down. 12.42 P.M., vomiting of food; the closing of eyes is less frequent; has a reeling walk. 12.55, respirations nine to twelve per minute. 1 P.M., eyelids nearly closed; feels and hears; staggers greatly; raises head with difficulty. 1.30 P.M., flapping of wings and great agitation, and then death ensues; spine not excitable; muscles are. When poles are placed over eye, the pupil contracts, and when removed it rebounds; no lesion discoverable.

Exp. VI.—3.10 P.M., rabbit received subcutaneously four cubic centimetres of fluid extract of gelsemium. 3.15 P.M., the extremities of feet lose their power, although the animal manages to locomote. 3.40 P.M., rolls backward on long axis; moves about; great difficulty in expiratory act; pupils dilated. 4.5 P.M., death. Right side of heart filled with blood; left side flaccid, and nearly empty; heart beating feebly.

The above experiments show that gelsemia is a respiratory poison ; that it attacks the motor ganglia, and finally the sensory, reversing the order as compared with cold-blooded animals.

EFFECT ON THE CIRCULATION.

That the method of experimentation may be better understood, I give a short résumé of cardiac physiology as taught at present.

The heart contains ganglia which send motor fibres to the cardiac muscle. In addition to motor ganglia there are other ganglia, called regulating ganglia, which co-ordinate the action of the heart, and act on the muscular fibres of the heart through the motor ganglia. The regulating ganglia oppose a certain resistance to the transmission of motor impulses to the cardiac muscle,—that is, governing the rhythm, and preventing the motor ganglia from exhausting themselves by irregular and excited action. Although the heart contains its own power of action, yet there are afferent and efferent nerves which play an important part in its movements: the pneumogastrics when irritated slow the pulse and augment its force, whilst the accelerators increase their number, but diminish their power. The pneumogastrics are especially excited by carbonic acid, decrement of temperature, and the sad emotions, whilst the accelerators are particularly thrown into action by the exhilarating emotions, increment of temperature, and oxygen. The brain also takes part in the regulation of the circulation through the vaso-motor centre situated in the medulla. This centre regulates the calibre of the small arteries, diminishing or increasing the amount of blood flowing through them. The cardiac afferent nerves just described can be thrown into increased action by sensations through the terminations of the sensory nerves in any section of the

body: hence the irritation of any portion of our skin can modify the amount of blood which flows through our body in a certain time, thus altering by necessity the functions of other organs. This fact explains the action of many external remedial agents, as baths, sinapisms, actual cautery, etc. The afferent nerve-fibres of the heart are the depressors of Ludwig and Cyon; they are the mechanism by which rupture of the heart by great arterial tension is avoided; as an excited action of the vaso-motor centre might cause. They convey the impulse from the heart to the vaso-motor centre which is paralyzed, and thus the small arteries are relaxed and the heart empties itself, the tension decreases, and everything works freely; they are the safety-valves of the heart, similar in function to those on steam-engines. These nerves also convey to the brain the sensations of a light, heavy, or palpitating heart.

In a pamphlet* published some time ago, I recorded some experiments on the circulation with an aqueous extract of gelsemium. As there were many other organic and inorganic bodies necessarily introduced with the gelseminate of gelsemia, the observations can only be of value as confirmatory of the action of the alkaloid. In the main they support the conclusions drawn from the following experiments. The circulation as influenced by this poison was studied on rabbits benumbed by sulphate of morphia, both in the interests of humanity and the experiment itself. The pulse and pressure were noted by Ludwig's mercurial manometer on the drum of his registering apparatus. The rate of movement was marked on the drum by an electro-magnet every second. By a lever attached to the electro-magnet the beginning and end of each injection were registered, as well as the time during

* Cocain, Veratria, and Gelsemium. Toxicological Studies, 1874.

which a nerve was irritated. The instruments used for irritation were one Grove cell eighty-one millimetres high and fifty-eight millimetres in diameter, Dubois-Reymond's induction apparatus, and Ludwig's electrodes. As the poison caused convulsive movements, curare was used to eliminate the action of the muscular system on the circulation. The gelsemia was injected towards the heart through the jugular or one of its branches, no air being allowed to enter; artificial respiration similar to normal was kept up, by an apparatus on the principle of Sprengel's blower, at regular intervals, by an electro-magnet and a metronome: the carotid artery was used for kymographic observations. The blood-pressure is given in millimetres of mercury, and the pulsations for periods of fifteen seconds.

Exp. I.—Rabbit; tracheotomy; jugular and carotid prepared; curare; artificial respiration.

Time.	Pulse.	Pressure.	
	60	102	
A.M.			Gelsemia .01 gramme.
9.25.00	60	88	
9.25.45	52	98	
9.26.45	55	99	
9.27.45	54	97	
9.49.45	56	90	
9.57.15	45	60	
9.59.00	52	50	
10.22.00	49	38	

Exp. II.—Small rabbit; tracheotomy; jugular and carotid prepared; curare; artificial respiration.

Time.	Pulse.	Pressure.	
	51	72	
P.M.			Gelsemia .01 gramme.
6.0.15	51	36	
6.0.30	50	32	
6.0.45	46	28	
6.1.00	45	22	
6.1.15	46	26	

Time.	Pulse.	Pressure.
6.2.45	46	23
6.3.00	45	23
6.3.45	44	26
6.5.00	48	24
6.6.15	46	25

The above experiments demonstrate that in gelsemia we have an agent which reduces the pulse and pressure, the latter greatly.

Now, physiologically, the pneumogastrics either by central or peripheral stimulation have the ability to reduce the pulse.

The pressure can be reduced by diminished tonus of the vaso-motor system or weakened heart.

That I might find out if gelsemia reduced the pulse-frequency by central stimulation of the pneumogastrics, they have been divided in the following experiment:

Exp. III.—Rabbit. Tracheotomy; carotid and jugular prepared; vagi cut; curare; artificial respiration.

Time.	Pulse.	Pressure.	
A.M.	51	92	
			Gelsemia .01 gramme.
11.36.30	51	53	
11.36.45	52	68	
11.37.15	48	46	
11.37.45	46	40	
11.38.30	44	28	
11.39.45	32	22	
11.46.15	38	18	
11.54.45	39	20	
11.55.00	33	16	Vagus irritated with Dubois secondary coil at 1 for six seconds; one Grove cell.
11.56.00	37	26	
12.00.15	40	36	Vaso-motor centre irritated indirectly with Dubois coil at 1 for fourteen seconds.

The same sequence of events takes place, so that gelsemia does not reduce the pulse through central stimulation of the pneumogastrics. In atropia we have an agent which is capable of removing the inhibitory power of the peripheral end of the vagi on the heart.

The succeeding experiment shows that even after paralysis of the inhibitory ganglia seated in the heart, gelsemia produces the same result.

Exp. IV.—Rabbit. Tracheotomy; vagi paralyzed by atropin, as tested by strong currents; curare; artificial respiration.

Time.	Pulse.	Pressure.	
P.M.	58	126	
			Gelsemia .01 gramme.
5.18.15	58	106	
5.18.30	52	106	
5.18.45	54	114	
5.19.15	50	126	
5.25.00	53	120	
5.37.40	50	94	
			Gelsemia .01 gr.
5.38.55	52	66	
5.39.10	47	55	
5.42.05	47	88	
5.46.20	50	80	
			Gelsemia .005 gr.
5.46.35	45	67	
6.02.53	42	66	
6.39.53	42	44	

To study the action of a poison on the heart itself, it is necessary to divide the afferent and efferent cardiac nerves in the neck (that is, the pneumogastrics, sympathetics, and depressors), and to remove the influence of accelerators and vaso-motor centre by section of the cord between the occiput and the atlas. In this manner the following experiment was performed:

Exp. V.—Rabbit. Tracheotomy; all the cardiac nerves in the neck cut; the cord divided between the atlas and occiput; the hemorrhage checked by bovista; curare; artificial respiration; section of cord verified by post-mortem.

Time.	Pulse.	Pressure.	
A.M.			
11.34.00	43	18	
			Gelsemia .01 gramme.
11.54.45	43	15	
11.36.00	42	15	
11.37.00	37	15	
11.38.00	37	15	
11.40.00	36	16	
11.41.00	37	16	
11.41.25	36	16	
			Gelsemia .01 gramme.
11.41.35	35	14	
11.42.35	34	13	
11.43.35	36	14	
11.44.35	34	13	

This experiment demonstrates that the cause of the slowing of the pulse resides in the heart itself, as well as part of the reduced pressure. Although the fall of pressure is partly to be explained by decrease of cardiac irritability, yet it is desirable to prove how far the vaso-motor nerves and the muscles in the arterial walls participate. When in the small blood-vessels the circular muscles relax, thus dilating the vessel, there is less blood flowing into the right ventricle, and consequently less into the left ventricle, which, by necessity, throws less blood into the arterial system than before in the same unit of time: consequently this is one factor of diminished pressure.

When the small arteries are dilated there is less resistance to the onward flow of blood, and, of course, less pressure in the arterial system, which is another factor.

When the pressure is diminished, according to the German school, the pulse is lessened. The grand agent in preserving the arterial pressure at its height is the vaso-motor centre. That the vaso-motor centre is not paralyzed to direct irritation the following experiment proves; but there is a probability that its tonus is lowered as the fall of pressure is greater, and more rapid when the centre is active than when its influence is removed.

Exp. VI.—Rabbit. Vagi paralyzed by atropin; tracheotomy; sciatic nerve prepared; Ludwig's gimlet-electrodes screwed into the atlas and occipital bone; Pohl's commutator used, so that the induced current could be sent either to the gimlet-electrodes or the electrodes bearing the sciatic by simply rolling the cradle.

Time.	Pulse.	Pressure.	
A.M.	55	80	
			Gelsemia .01 gramme.
10.35.15	53	70	
10.35.45	52	78	Vaso-motor centre irritated directly for two seconds; secondary coil at 8.
10.38.24	52	50	
			Gelsemia .01 gramme.
10.38.39	51	31	
10.38.54	47	18	
10.39.19	52	18	
10.39.34	53	72	
10.54.11	43	5	
10.54.26	42	3	Depressor nerve irritated eight seconds; Dubois coil at 8.
10.58.30	48	8	
11.06.45	46	22	Vaso-motor centre irritated directly for eight seconds; Dubois coil at 8.

The deductions from the above experiments are:

1. That gelsemia reduces the pulse and the pressure; the latter greatly.

2. That the pneumogastrics are not affected by it.

3. That it reduces the pulse by an action on the heart itself, probably through a paralyzing action on the excito-motor ganglia.

4. That it reduces the pressure through diminished cardiac irritability and decreased vaso-motor tonus.

5. That the functions of the depressor are not interfered with.

ACTION ON THE RESPIRATION.

Exp. I.—Rabbit. T-shaped tube in trachea; jugular prepared; Marey's polygraph registering respiration on Ludwig's drum; the rapidity of the movement of drum being noted by an electro-magnet, marking seconds.

Time.	Resp. for 15″.	
	16	
		Gelsemia .01 gramme.
4.34.00	19	Struggle, convulsive movement.
4.34.15	16	
4.34.30	12	
4.34.45	12	
4.35.15	11	
4.36.45	11	
4.37.00	11	
4.40.15	11	
4.53.21	11	
5.01.40	11	
		.005 gramme gelsemia.
5.01.55	11	
5.02.55	10	Convulsive movements.
5.03.35	11	
5.05.15	9	Opisthotonos.
		Gelsemia .01 gramme injected.
5.05.30	12	
5.05.45	11	
5.08.00	7	
5.14.00	6	
5.25.15	1	

The above observation shows that gelsemia gradually reduces the number of respirations. The paralyzing effect on the respiratory centres is the cause of this action, as the poison does not attack either the pneumogastrics, the striated muscles, or the motor nerves.

ACTION ON THE TEMPERATURE.

The following experiment was made with a specimen of gelsemia furnished by Charles McIntire, Jr., formerly Assistant Professor in Lafayette College. The temperature is rectal.

Exp. I.—2 P.M., kitten received subcutaneously .004 gramme of gelsemia in shape of chloride. 2.05 P.M., weakness in posterior extremities; trembling of head and ears; pupil in diameter five millimetres; temperature 101⅔° Fahr. 2.25 P.M., .002 gramme gelsemia. 2.37 P.M., sinking down on fore-legs, drooping of head, difficult expiration. 2.45 P.M., temperature 101 8/10°, pupils same. 2.50 P.M., cries, makes staggering efforts to walk, but sinks into a prone position; backward movements; no co-ordinating power; sphincters give way. 3.40 P.M., .004 gramme gelsemia. 3.55 P.M., temperature 100 3/10°; pupil five millimetres. 4.25 P.M., .004 gramme. 4.56 P.M., pupil six millimetres; .002 gramme gelsemia; temperature 99 1/10°. 5.5 P.M., pupil seven millimetres; reflex movement in cornea. 5.10 P.M., .004 gramme gelsemia; death; chest opened; auricles beating, but not ventricles; intestinal peristalsis present; cord not excitable; muscular irritability good; no reflex action; heart excitable when electricity applied.

Exp. II.—Rabbit. Temperature 103⅖° per rectum. 8.40 A.M., received subcutaneously 2½ cubic centimetres of fluid extract of gelsemium. 8.45 A.M., temperature 103½°. 8.52 A.M., four cubic centimetres fluid extract gelsemia. 9 A.M., temperature 103½°. 9.12 A.M., temperature 102⅖°. 9.45 A.M., temperature 101½°. 10.20 A.M., injection four cubic centimetres fluid extract gelsemium. 10.30 A.M., temperature 99°. 11 A.M., 98¾°. 11.5 A.M., animal dead.

These experiments show that gelsemia reduces the temperature.

To make more complete and practical the study of the action of gelsemia, I give the following experiments on man,—cases of poisoning. Substantially they are as follows:

Case I.—Reported by R. P. Davis. Lying on left side; muscular relaxation; face somewhat congested; double vision; vertigo; pupils dilated, but responding to different degrees of light; eyelids half closed, with apparent inability to move them; lower jaw drooping; his tongue, to use his own expression, "so thick that he could hardly speak;" skin warm and moist; pulse small and feeble; neither purging nor vomiting; respirations diminished; great numbness of the extremities; surface cold and congested; pulse almost imperceptible. Death took place in about two hours and a half after taking a tablespoonful of Tilden's fluid extract; unconsciousness preceding death for an hour.

Case II.—Reported by R. P. Davis. After same dose, double vision, vertigo, pupil widely dilated, complained of blindness, staggered in walking, deep inspirations, and numbness of whole body; no loss of consciousness at any time; awoke next morning weak and dizzy. The patient in the first case was a very small, nervous, delicate man; the second case was the reverse, and, besides, he received an emetic soon after taking the poison.

Case III.—Prof. Wormley reports the following case: Young married woman, pregnant, took three teaspoonfuls of Tilden's fluid extract. In two hours complained of pain in stomach, nausea, and dimness of vision. These symptoms were followed by great restlessness, ineffectual efforts to vomit, and free perspiration over the body. At the end of five hours pulse feeble, irregular, and sometimes intermittent; great prostration, irregular and slow res-

piration; skin dry, extremities cold, pupils expanded and insensible to light; eyes fixed, and inability to raise the eyelids. Death occurred in about seven hours and a half after taking the poison. No convulsions preceding.

Prof. Wormley thinks that these three teaspoonfuls could not have contained more than a sixth of a grain of the alkaloid.

Case IV.—Reported by Dr. Main. He took one drachm of fluid extract of gelsemium. Nearly blind; control over upper eyelids was almost entirely lost; flexor muscles of hands and arms paralyzed; extensors nearly so; sensation in hands and arms blunted, but not in proportion to loss of motion. Before muscles affected, disagreeable sensation in head; mind clear; hands suffered more than the legs.

Case V.—Reported by Dr. Freeman, of Brooklyn. Boy, æt. three years. After taking fifty minims of tincture of gelsemium (made by maceration of four ounces of the root to a pint of dilute alcohol), died in two hours. The symptoms were double vision, staggering gait, complete muscular relaxation.

Case VI.—Reported by Dr. Freeman. Girl, æt. nine years; after dessertspoonful of tincture, had dimness of vision, loss of muscular power, and death in less than two hours.

Case VII.—Reported by Dr. Freeman. Boy, æt. about three years, was to take a teaspoonful every two hours of a mixture containing ten grains of sulphate of quinine, a drachm of tincture of gelsemium, and five drachms of syrup. After first dose, prostration, staggering; in about half an hour after second dose, limp as a rag; pupils dilated, froth, heart beating feebly and slowly, pulse imperceptible at the wrist, could not swallow. Death in about an hour after the second dose.

Case VIII.—Reported by Dr. Pinkham, of Lynn. Double vision, blindness, numbness, oppression, unconsciousness, stertorous, very imperfect breathing, countenance lividly pale, lower jaw drooping, leaving mouth wide open; eyelids partially closed, motionless; pupils moderately dilated; pulse 100 per minute, regular, weak. After friction and stimulus for an hour and a half, consciousness returned, but recovery was not complete for several days, the principal complaint being great prostration, muscular weakness, particularly of the elevators of the lower jaw, eyelids, and muscles of arm. After the return of consciousness, speech was intelligible only when the jaws were supported. The tongue during the poisoning was stiff, and voice guttural. The dose was pretended to be forty minims of fluid extract, and the patient was a woman.

Case IX.—Reported by Dr. Boutelle, of Boston. Man, æt. twenty-four, at 1 A.M. took a teaspoonful of Tilden's fluid extract of gelsemium. In fifteen minutes he repeated the dose; his pain was soon relieved; eyes felt heavy, and in about half an hour complained of choking; soon arose, struggling for breath, pushing his fingers into his throat as if trying to tear it open. He staggered reeling from one room to the other, as though intoxicated, and shortly afterwards threw himself on the floor, and became unconscious. 4 A.M., respirations gasping, three or four per minute; pulse rapid and feeble; unconscious, could not be roused; pupils dilated, not responding to light; eye could be touched without any contraction of the lids; skin moist; extremities cold; pulse grew slower and weaker. Death in three hours and forty-five minutes after taking the poison, without any convulsions occurring at any time.

An analysis of the above cases of poisoning gives the following as the course of symptoms: Disor-

dered double vision, ptosis, want of co-ordination in the movements, disagreeable feeling in the head, great muscular relaxation, lower jaw drooping, tongue stiff, sensation blunted, pupils dilated, respiration slow and irregular, pulse slow and feeble, surface cold and congested, unconsciousness, and death.

On comparison of its effects on man and warm-blooded animals, the analogy is complete. In man there is the same paralysis of motion, want of co-ordination, diminished sensibility, relaxation of muscles of the jaws and the rest of the body, diminished pulse and pressure, lessened respiration, decreased temperature, and dilated pupils.

The following résumé expresses our conclusions in regard to gelsemia:

1. In cold-blooded animals it paralyzes first the sensory ganglia, and then the motor ganglia in the central nervous system. This order is reversed in warm-blooded animals.

2. It diminishes the pulse and pressure.

3. This decrease of pulse-rate is due to lessened irritability of the excito-motor ganglia of the heart.

4. The fall of pressure is due to diminution of cardiac irritability and vaso-motor tonus.

5. It decreases the respiration through a paralyzing action on the respiratory centres.

6. It dilates the pupils.

7. It reduces the temperature.

The above investigation was made in the Physiological Laboratory of Prof. F. G. Smith, University of Pennsylvania.